UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,663	08/03/2001	Philippe Pouletty	500862000105	8307

20872 7590 10/19/2004

MORRISON & FOERSTER LLP
425 MARKET STREET
SAN FRANCISCO, CA 94105-2482

EXAMINER	
GUPTA, ANISH	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/921,663	POULETTY ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8-2-04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-34* is/are pending in the application.

4a) Of the above claim(s) *13-22,24,25,27-29 and 31-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,23,26,30 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

1. Applicant's election of X as the antiproliferative agent, Y is about 24 atoms linker, and Z is a maleimide group, dated 3/18/04, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants argued that they did not elect a sub-species of chemotherapeutic agents since a antiproliferative agent is a species of a generic "target entity." As explained to applicant in the interview, dated 2/19/04, that Applicants election will be accepted to further prosecution. However, the application will be examined to the point where a species reads on the generic election of X as the antiproliferative agent, Y is about 24 atoms linker, and Z is a maleimide group. The search will not be extended unnecessarily to cover all of the species covered by the election. If Applicants overcome the rejection in the next response, the prior art search will be extended to the extent necessary to determine patentability of the Markush-type election. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claims, reading on the species will be rejected and the action made final.

In the instant office action, prior art was found on the Markush type election. Claims 13, 23, 26, 30, 34 read on the prior art and have been rejected. Claims 13-22, 24-25, 27-29, 31-33 have been withdrawn from consideration.

Note that this application contained issues associated with 112 First paragraph. These claims have only been examined to the extent of 112 First paragraph issues and not prior art issues. Hence, even though they were included in the 112 rejection below, the claims are still held withdrawn from consideration as being drawn to being drawn to a non

elected invention. These claims were included in the 112 First paragraph rejection to assist in furthering of prosecution.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 13-34 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that support for the amended claims can be found on page 3, lines 18-20, of the specification where it is stated 'a first compound comprising a chemically reactive entity which is capable of forming covalent bonds with functionalities present on proteins, joined by a covalent bond or a first linking group to an agent." Applicants assert that linking group and linking entity are used interchangeably and "antiproliferative drug" provides support as an agent or compound of interest. Thus, the specification provides support for the claimed invention.

Applicants response has been considered by has not been found persuasive.

The instant claims recite the compound comprise a therapeutic agent, chemical reactive entity, where the chemical reactive entity is linked via a in-vivo cleavable lining

entity. Later claims recite that the reactive entity include N-hydroxysuccinimide, carbodiimide anhydride, N-hydroxysulfosuccinimide, and maleimide. Note that in the election, dated3/18/04, Applicant specifically elected the maleimide group as the chemical reactive entity.

The specification discloses a first compound comprising a chemical reactive entity that is linked to an agent of interest with a linking entity. Applicants have stated that the agent of interest includes antiproliferative drugs, thereby satisfying the thereapeutic agent of the claimed invention. Applicants also assert that the linking entity and the linking group is interchangeable. However, the specification fails to teach or disclose maleimide as a chemically reactive entity, i.e. the first compound. The specifications illustrates that first compounds as hydroxysulfosuccinimydyl biotin ester, N-hydroxysulfosuccinimidyl ester of N-biotinyl 6-aminohexanoic, N-hydroxysulfosuccinimidyl ester of biotinyl 4-butyryl, 3-aminoporpyl disulfide, and the like (see page 7 of the specification). The specification does not provide support that the first compound or chemical reactive be a carbodiimide anhydride, N-hydroxysuccinimide or N-hydroxysulfosuccinimide (note that the specification states tat hydroxysulfosuccinimydyl are esters of biotin and not N-hydroxysuccinimide or N-hydroxysulfosuccinimide themselves.). It is acknowledged that the specification does exemplify maleimide and N-hydroxysuccinimide on page 5 of the specifcation. However, these are used on the context of linking entities and not first compounds of chemical reactive entities.

Thus, the claims still lack written description in the originally filed specification.

Prior art Rejections

3. Applicants state that U.S. patent application 07/592,214 is a continuation of 08/237,346 and has an identical specification. Applicants assert that the "present application therefore has a priority date of at least May 3, 1994."

Applicants arguments have been considered but have not been found persuasive.

Applicants elected maleimide as a chemical reactive entity. The specification, of parent application 09/539766 or 08/477,900 (Patent No. 6103233), do not disclose the use of a maleimide compound as a chemically reactive entity. The only context in which malemide groups are disclosed are in the use of linking agents, similar to the instant application. Thus, priority to the parent applications is denied.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 13, 23, 26, 30, 34 remain rejected under 35 U.S.C. 102(a) as being anticipated by Kratz et al. (WO 00/76550).

The claims are drawn to a compound of that comporises an antiproliferative drug, a linker of 9 atoms in the chain, and a maleimide group as a chemical reactive entity.

The reference discloses maleimide derivatives of doxorubicin (see page 26). The reference discloses a doxorubicin conjugated to a maleimide using the peptide QGAIFLPG. The doxorubcin is the antiproliferative drug, since it is a cytotoxic agent for tumor cells. Finally, the amino acid length leads to an exact 24 atoms in the peptide backbone, thereby meeting the limitation of Y. Thus, the reference anticipates the claimed invention.

The rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 13, 23, 26, 30, 34 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Someno et al.

The claims are drawn to a compound of that comprises an antiproliferative drug, a linker of 9 atoms in the chain, and a maleimide group as a chemical reactive entity.

Applicants argue that the reference fails to teach that maleimide "reacts in vivo with a reactive functionality on an endogenous vascular or blood component protein to form a covalent bond therewith, as required by the claims." Applicants then make a distinction between the disclosure of the binding of antibodies to the complex and blood proteins. Further, the reference fails tot teach that a chemical reactive entity forms a covalent bond

with a reactive functionality elected from the group consisting of amino, carboxylate or thiol reactive functionality. Next, the reference fails to teach that the polylysine groups are cleavable in-vivo. Further, the rejection fails to provide the requisite motivation to alter the teaching of the references. The reference fails to provide any motivation or suggestion for one skill in the art to form a covalent bond between maleimide and reactive functionality and cleave the poly lysine in-vivo. Finally, there is no reasonable expectation of success in modifying the teachings to come across the claimed invention. "The cited provides no teaching that would provide one ordinary skill with a reasonable expectation of bonding maleimide to a reactive functionality of the endogenous vascular or blood component protein, forming a covalent bond between maleimide and reactive functionality selected from the group consisting of an amino, carboxylate, or thiol, or cleaving polylysine in vivo."

Applicants arguments have been considered but not found persuasive.

The MPEP states:

> Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433.

Here, as stated in the previous office action, the reference discloses all of the structural limitation of the claims, including the covalent linkages that Applicants dispute. The reference disclose a "peplomycin-polylysine-maleimide complex." By virtue being a complex, each component must be complexed to the other two. This can be achieved by,

covalent linkage or non-covalent linkage (ionic, hydrogen bonding or vanderval forces). The fact that lysine residues have a free amine and a free carboxyl group, one could readily conclude that one of those functionalities were used in forming the complex. The STN print out, furnished to Applicants in the previous office action, show the structure of polylysine used in the complex. Note that the structure has a free carbonyl and a free amine native the peptide backbone. These are the functionalities used to form the complex. Thus a chemical reactive entity has to form a covalent bond with a reactive functionality selected from the group consisting of amino, carboxylate or thiol reactive functionality.

The arguments regarding in-vivo cleavage and reaction with blood components also do not have merit. As stated above, "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established." Here all of the structural limitations have been met, it is Applicants burden to prove that prior art products do not necessarily possess the characteristics of the claimed product.

Rejection is maintained.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened

statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can normally be reached on (571) 272-0974. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta 10/13/04
Patent Examiner

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600